Potential cytochrome P450–mediated drug-drug interactions with selective serotonin reuptake inhibitors: A retrospective analysis of a university hospital prescription database

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Abstract

Rationale, aims and objectives The study aimed to investigate the rate of the potential cytochrome P450 (CYP450)-mediated drug-drug interactions (DDIs) between selective serotonin reuptake inhibitors (SSRI) and other drugs, and identify the most common CYP450-interacted SSRI-drug combinations in real-life clinical practice. Methods This is a retrospective analysis of SSRI prescribing data from the Akdeniz University Hospital database, a tertiary hospital database in Turkey. Prescriptions which were included an SSRI had been selected (from January 2014 to December 2018). Lexicomp® Online was used to identify potential CYP450-mediated DDIs. Results A total of 7.5% of SSRI prescriptions were at risk of potential CYP450-mediated DDIs; 74.4% (n = 67) of the pDDIs were identified as category D modification of treatment should be considered. Antipsychotics were involved in 71.8% category D potential DDIs and 83.6% category C potential DDIs. The medications most frequently identified in combination with SSRIs were risperidone (31.7%) and aripiprazole (31.6%). Finally, CYP2D6 and CYP3A4 were the two most commonly affected CYP450 isozymes. Conclusions Prescribing antipsychotic-SSRI pairs interacting via CYP450 may increase serum concentrations of antipsychotics. Using DDI alert software while writing electronic prescriptions during clinical practice may reduce the frequency of ADRs.

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CYP450 interactions in SSRI prescriptions

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Methods

This is a retrospective analysis of SSRI prescribing data from the Akdeniz University Hospital database, a tertiary hospital database in Turkey. Prescriptions which were included an SSRI had been selected (from January 2014 to December 2018). Lexicomp® Online was used to identify potential CYP450-mediated DDIs.

Results

A total of 7.5% of SSRI prescriptions were at risk of potential CYP450-mediated DDIs; 74.4% (n = 67) of the pDDIs were identified as category D modification of treatment should be considered. Antipsychotics were involved in 71.8% category D potential DDIs and 83.6% category C potential DDIs. The medications most frequently identified in combination with SSRIs were risperidone (31.7%) and aripiprazole (31.6%). Finally, CYP2D6 and CYP3A4 were the two most commonly affected CYP450 isozymes.

Conclusions

Prescribing antipsychotic-SSRI pairs interacting via CYP450 may increase serum concentrations of antipsychotics. Using DDI alert software while writing electronic prescriptions during clinical practice may reduce the frequency of ADRs.

Keywords

drug interactions; selective serotonin reuptake inhibitors; cytochrome P450; prescription

Introduction

Antidepressants are one of the most widely prescribed drugs with an increasing trend in use during the past decades [1]. Besides the introduction of selective serotonin reuptake inhibitors (SSRIs), the rise in use has also been explained by the prolongation of treatment duration of antidepressants [2]. In addition to major depression, SSRIs are also indicated for a wide range of psychiatric disorders, including obsessive-compulsive disorder, posttraumatic stress disorder, panic disorder, generalized anxiety disorder, and eating disorders [3]. Long-term use of antidepressants puts the treatment at increasing risk of co-administration with other drugs in time, which can result in toxicity or reduced efficacy via drug-drug interactions (DDIs)[2].

DDIs are common preventable causes of adverse drug reactions (ADR), which can occur at the pharmacodynamic or pharmacokinetic level[4]. Since cytochrome P450 (CYP450) isoenzymes responsible for the metabolism of many antidepressants, CYP450-mediated pharmacokinetic DDIs are frequently seen among antidepressant users[5]. Several antidepressants can markedly inhibit different CYP450 enzyme activities or could be a substrate for them[5]. Compared with the other antidepressant groups, SSRIs usually inhibit one or more CYP450 isozyme moderately to substantially at their therapeutic doses [6]. Also, it has been known that the large inter-individual variability observed in serum concentrations of SSRIs results mainly from variation in the activities of CYP450 enzymes [7]. Besides, SSRIs display differences in their potential for CYP-mediated DDIs due to the inhibition capacities on CYP450 enzymes [8]. Therefore, avoiding co-administration CYP450 interacting drugs with SSRIs could reduce ADRs via preventing CYP450-mediated DDIs.

In the literature, little is known about the frequency and severity of CYP450-mediated DDIs among SSRIs users. Almost all prior studies have examined all the DDIs in broad psychiatric populations. In this study, we focused on potential CYP450-mediated DDIs in prescriptions of SSRIs. Therefore, we aimed to examine the reciprocal potential CYP450-mediated DDIs between the SSRIs and other drugs in terms of frequency and severity.

Methods

Study design

This was a retrospective cross-sectional study performed at a tertiary hospital in Turkey. The study was approved by the Akdeniz University Clinical Research Ethics Committee (2019-421-05).

Procedures

All SSRI prescriptions stored electronically in the Akdeniz University Hospital database between January 2014 and December 2018 were assessed. Data evaluated for CYP450-mediated DDIs potential according to the Lexi-Interact Online database. DDIs are categorized into five groups depending on their severity of clinical significance. The recommendations of the database for per category of DDIs as (A) No known interaction; (B) No action needed; (C) Monitor therapy; (D) Consider therapy modification; (X) Avoid combination. Potential CYP-mediated drug-drug interactions were classified as category X, D, and C, using according to Lexicomp(r) Online.

Statistical Analysis

All data were analyzed using descriptive statistics. Data were expressed as frequency and percentage.

Results

Potential CYP450-mediated DDIs rates in SSRI prescriptions

A total of 7.5% (n=3.318) of all SSRI prescriptions (n=44.081) were associated with CYP450-mediated DDIs potential. Based on the Lexi-Interact Online database, about 74.4% of interactions belonged to category D, 25.4% were at category C and 0.2% were at category X (Table 1). In all SSRI prescriptions, the rate of D and C type DDIs was 5.6% and 1.9%, respectively (Table 1).

The majority of potential CYP450-mediated interactions were identified in fluoxetine (50.9%), paroxetine (26.4%), and sertraline (13.4%) prescriptions, whereas the rest were identified in escitalopram (4.5%), fluvoxamine (3.7%), citalopram (1.1%) prescriptions (Table 2). D type interactions were frequently prescribed with fluoxetine (62.8%) and paroxetine (29.6%). However, most C type interactions involved in sertraline prescriptions (52.6%) (Table 3).

We next investigated the ratios of CYP450-mediated interaction potentials for each SSRI, separately. Among all SSRIs, fluvoxamine (21.6%), paroxetine (18.3%) and, fluoxetine (17.8%) prescriptions were with the high risk for the potential of CYP450-mediated DDIs, whereas prescriptions including escitalopram (1.1%), sertraline (3.0%), and citalopram (4.4%) were at low risk of the potential (Table 2). In terms of DDIs category, fluoxetine (16.4%) and paroxetine (15.3%) prescriptions were at high risk for D type interaction and, prescriptions of fluvoxamine (12.9%) were at the highest risk of potential for C type interaction. Prescriptions that involved category X (n=7) belonged to fluvoxamine and fluoxetine; 6 of them fluvoxamine and, only 1 of them fluoxetine.

Most frequent potentially CYP450-mediated interacted drugs with SSRIs

The most common potentially interact drug group was antipsychotics (n=2481, 74.8%) followed by other antidepressants (n=325, 9.8%), beta-blockers (n=325, 6.9%) and, antiepileptics (n=135, 4.1%) (Figure 1). Antipsychotics were associated with 71.8% (n=1775) of all category D interactions and 83.6% (n=706) of C category interactions. Among antipsychotics, the two most frequent interact drugs were risperidone (n=1051, 42.4%) and aripiprazol (n=1047, 42.2%).

Table 4 presents the drug pairs that most frequently involved category D&C interactions. Fluoxetine-risperidone combination was the most common interactions in category D, accounting for 31.1% of all D type interactions, the rest were fluoxetine combined with aripiprazole (16.8%), paroxetine combined with risperidone (11.4%), paroxetine combined with aripiprazole (5.9%) and, paroxetine combined with mirtazapine (4.6%). Among the most common drug pairs in category C, the most five dispensed combinations were sertraline combined with aripiprazole (46.9%), paroxetine combined with clozapine (14.1%), fluoxetine combined with clozapine (12.1%), fluvoxamine combined with aripiprazole (9.1%) and, sertraline combined with carbamazepine (5.6%).

Most frequent affected CYP450 enzymes from pDDIs in SSRIs prescriptions

In the present study, a total of 37 different drugs potentially interacted with SSRIs via at least one CYP450 enzymes (Supplementary data). Besides, CYP450-interact 64 different drug pairs were determined in pDDIs prescriptions (Supplemental data). The most interact CYP450 isoenzyme was CYP2D6 (n=2958) followed by CYP3A4 (n=305), CYP2C9/19 (n=51) and, CYP1A2 (n=44) (Table 5). The majority of CYP2D6-mediated pDDIs were determined in fluoxetine prescriptions (n=1674, 56.6%). Escitalopram was associated with 49.2% (n=150) of all CYP3A4-mediated pDDIs. All of the CYP1A2-mediated pDDIs were identified in fluvoxamine prescriptions (n=44). Similarly, all of the CYP2C9/19-mediated pDDIs were identified in fluoxetine prescriptions (n=51).

Discussion

SSRIs, a commonly prescribed antidepressant group, could produce clinically significant inhibition of one or more CYP450 isozymes[9]. Nevertheless, polypharmacy with SSRIs is recommended for several psychiatric disorders by clinical guidelines[10], the insufficient evidence on treatment modifications related to DDIs as a consequence of polypharmacy[11]. While pharmacokinetic DDIs are often predictable, knowledge of the rate, level, clinical magnitude of CYP-mediated DDIs between SSRIs and other drugs is essential. Thus, it is important to know of CYP-mediated DDIs in SSRI prescriptions in terms of most prescribed SSRI, drugs that interacted with SSRIs, and common drug pairs.

Earlier studies have examined CYP450-mediated pDDIs in SSRI prescriptions specifically, covered only fluoxetine, paroxetine, and sertraline, have shown higher rates for interactions[12,13]. In the first study mentioned earlier, the concomitant use of CYP2D6/3A4 metabolized medications in patients who were also receiving fluoxetine, paroxetine or sertraline were detected as 25.5% [12]. The second study, by Preskorn et al., found 11% of the potential to cause CYP-mediated DDIs in patients taking fluoxetine, paroxetine, or sertraline [13]. In the present study, we have shown the rate of CYP450-mediated pDDIs for all CYP450 isoenzymes in fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, and escitalopram prescriptions as 7.5% in a tertiary hospital.

It is important to point out that in this study Category D interactions constituted 74.4% of all CYP-mediated interactions. Also, antipsychotics are the most commonly identified CYP-mediated interacted drug group in D category (71.8%). Among the antipsychotics, risperidone (42.4%) and aripiprazole (42.2%) were the two most frequently interacted drugs. Thus, modification of drug therapy is needed when using SSRIs and risperidone/aripiprazole concomitantly.

Our results have shown that approximately half of the potential CYP450-mediated interactions were prescribed with fluoxetine (50.9%). For nearly 40 years, different formulations of fluoxetine as a strong inhibitor of CYP2D6 and CYP2C9 have been prescribed for many psychiatric disorders [14]. Also, a majority of pDDIs (91.9%) determined in fluoxetine SSRI prescriptions fell into category D, which most frequently combined with risperidone and aripiprazole. Co-administration of fluoxetine with risperidone or aripiprazole can cause significant elevations in the serum levels of risperidone and aripiprazole metabolized via CYP2D6 [15,16,17]. When considering prescribing fluoxetine to patients currently taking risperidone/aripiprazole or vice versa, it is reasonable to reduce risperidone/aripiprazole doses[11].

Our findings are consistent with previous research concerning the most common interacted CYP enzymes

were CYP2D6 and CYP3A4 in SSRI prescriptions. In a study, Gregor et al. reported that 25.5% of patients treated with fluoxetine, paroxetine, and sertraline experienced concomitant use with at least one CYP2D6 or 3A4 metabolized drug[12]. Similarly, Preskorn et al. observed that of all patients receiving fluoxetine and/or paroxetine, 8% were also receiving a potential CYP2D6-interacted drug with a narrow therapeutic index[13]. Furthermore, a study which investigated CYP-mediated pDDIs in all psychiatric population has shown that CYP2D6 and CYP3A4 are the most affected CYP isoforms [18]. These results are explainable by the fact that SSRIs inhibit predominantly CYP2D6 isoform and CYP2D6/3A4 isoforms metabolize a major part of SSRIs.

Our analysis concluded that there are also other safer SSRI-drug pairs not interacted at least via other CYP isoenzymes (Table 6). In this study, risperidone or aripiprazole was frequently combined with fluoxetine or paroxetine (Table 4). But, these combinations may lead to an increase in serum concentrations of risperidone and aripiprazole via inhibition of CYP2D6 [15,19,20,21]. If therapeutic efficiency is sufficient in combination with risperidone or aripiprazole, it seems to add on SER, ESC, FLV, CIT instead of fluoxetine or paroxetine is safer [22,23,24,25]. Add on olanzapine to fluoxetine or paroxetine treatment is another choice for a safer drug combination in terms of CYP-mediated drug interactions[26].

There are some limitations of the current study. First, the study was limited to analyzing prescriptions dispensed in a university hospital, and therefore, the results may not reflect all clinical practice. Second, we evaluated only CYP-mediated DDIs specifically, pharmacodynamic interactions or other types of pharmacokinetic DDIs were not included. Therefore, we cannot recommend another drug pair instead of interacting combinations in this study. Furthermore, we used only Lexi-comp to identification DDIs. Thus, it is likely that these findings may differ if we use another source for drug interactions. Additionally, our data contained the drugs solely in the same prescriptions, not all medications the patient used. Thus, it was not possible to find the rate of DDIs for each patient. Because the e-prescriptions only included information about the medication prescribed, the daily dose of drugs could not be evaluated in terms of DDIs potential.

In summary, as the CYP isoenzymes playing a major role in the metabolism of SSRIs, avoiding the use of SSRI&CYP-interacted drug combinations is a rational strategy for diminishing CYP-mediated pDDIs during the SSRIs therapy. Since most of the CYP-mediated pDDIs fell into category D, it seems that concomitant prescription of SSRIs and risky drugs could result in ADRs. Our results may help physicians to identify and avoid the frequent CYP-interacted SSRI-drug combinations in a real-life setting. Further studies are needed to assess the rate of pDDIs for all medications a patient uses.

Key points

- 7.5% of SSRI prescriptions were associated with CYP450 mediated DDI potential
- Majority of prescriptions with CYP450-mediated pDDIs were fell into category D
- Approximately half of prescriptions with CYP450 mediated pDDIs were fluoxetine prescriptions
- Antipsychotics were associated with approximately three-quarters of CYP450-mediated pDDIs

Declaration of Interest

The authors declare that they have no conflicts of interest.

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References

1. Kendrick T. Strategies to reduce use of antidepressants. *Br J Clin Pharmacol* . Published online 2021. doi:10.1111/bcp.14475

2. McCrea RL, Sammon CJ, Nazareth I, Petersen I. Initiation and duration of selective serotonin reuptake inhibitor prescribing over time: UK cohort study. *Br J Psychiatry* . Published online 2016. doi:10.1192/bjp.bp.115.166975

3. Degli Esposti L, Piccinni C, Sangiorgi D, Fagiolini A, Buda S. Patterns of Antidepressant Use in Italy: Therapy Duration, Adherence and Switching. *Clin Drug Investig* . Published online 2015. doi:10.1007/s40261-015-0332-4

4. Magro L, Moretti U, Leone R. Epidemiology and characteristics of adverse drug reactions caused by drugdrug interactions. *Expert Opin Drug Saf* . Published online 2012. doi:10.1517/14740338.2012.631910

5. Hiemke C, Bergemann N, Clement HW, et al. Consensus Guidelines for Therapeutic Drug Monitoring in Neuropsychopharmacology: Update 2017.*Pharmacopsychiatry* . Published online 2018. doi:10.1055/s-0043-116492

6. Wyska E. Pharmacokinetic considerations for current state-of-the-art antidepressants. *Expert Opin Drug Metab Toxicol* . Published online 2019. doi:10.1080/17425255.2019.1669560

7. Spina E, de Leon J. Clinical applications of CYP genotyping in psychiatry. *J Neural Transm* . Published online 2015. doi:10.1007/s00702-014-1300-5

8. Hemeryck A, Belpaire F. Selective Serotonin Reuptake Inhibitors and Cytochrome P-450 Mediated Drug-Drug Interactions: An Update. *Curr Drug Metab* . Published online 2005. doi:10.2174/1389200023338017

9. Preskorn SH. Drug-Drug Interactions (DDIs) in Psychiatric Practice, Part 9: Interactions Mediated by Drug-metabolizing Cytochrome P450 Enzymes. *J Psychiatr Pract* . Published online 2020. doi:10.1097/PRA.0000000000000458

10. Rhee TG, Mohamed S, Rosenheck RA. Antipsychotic prescriptions among adults with major depressive disorder in office-based outpatient settings: National trends from 2006 to 2015. *J Clin Psychiatry* . Published online 2018. doi:10.4088/JCP.17m11970

11. Rhee TG, Rosenheck RA. Psychotropic polypharmacy reconsidered: Between-class polypharmacy in the context of multimorbidity in the treatment of depressive disorders. *J Affect Disord* . Published online 2019. doi:10.1016/j.jad.2019.04.018

12. Gregor KJ, Way K, Young CH, James SP. Concomitant use of selective serotonin reuptake inhibitors with other cytochrome P450 2D6 or 3A4 metabolized medications: How often does it really happen? *J Affect Disord* . Published online 1997. doi:10.1016/S0165-0327(97)00080-3

13. Preskorn SH, Shah R, Neff M, Golbeck AL, Choi J. The potential for clinically significant drug-drug interactions involving the CYP 2D6 system: Effects with fluoxetine and paroxetine versus sertraline.*J Psychiatr Pract* . Published online 2007. doi:10.1097/00131746-200701000-00002

14. Wong DT, Perry KW, Bymaster FP. Case history: The discovery of fluoxetine hydrochloride (Prozac). *Nat Rev Drug Discov* . Published online 2005. doi:10.1016/j.ajo.2005.02.011

15. Spina E, Avenoso A, Scordo MG, et al. Inhibition of risperidone metabolism by fluoxetine in patients with schizophrenia: A clinically relevant pharmacokinetic drug interaction. *J Clin Psychopharmacol* . Published online 2002. doi:10.1097/00004714-200208000-00014

16. Duggal HS, Kithas J. Possible neuroleptic malignant syndrome with aripiprazole and fluoxetine [2]. *Am J Psychiatry* . Published online 2005. doi:10.1176/appi.ajp.162.2.397-a

17. Bostankolu G, Ayhan Y, Cuhadaroglu F, Yazıcı MK. Serotonin syndrome with a combination of aripiprazole and fluoxetine: A case report.*Ther Adv Psychopharmacol* . Published online 2015. doi:10.1177/2045125314561467

18. Hefner G, Wolff J, Hahn M, et al. Prevalence and sort of pharmacokinetic drug–drug interactions in hospitalized psychiatric patients. *J Neural Transm* . Published online 2020. doi:10.1007/s00702-020-02214-x

19. Mannheimer B, Von Bahr C, Pettersson H, Eliasson E. Impact of multiple inhibitors or substrates of cytochrome P450 2D6 on plasma risperidone levels in patients on polypharmacy. *Ther Drug Monit* .

Published online 2008. doi:10.1097/FTD.0b013e31818679c9

20. Spina E, Avenoso A, Facciolà G, Scordo MG, Ancione M, Madia A. Plasma concentrations of risperidone and 9-hydroxyrisperidone during combined treatment with paroxetine. *Ther Drug Monit* . Published online 2001. doi:10.1097/00007691-200106000-00007

21. Nemoto K, Mihara K, Nakamura A, et al. Effects of paroxetine on plasma concentrations of aripiprazole and its active metabolite, dehydroaripiprazole, in Japanese patients with schizophrenia. *Ther Drug Monit* . Published online 2012. doi:10.1097/FTD.0b013e31824a31e6

22. Spina E, D'Arrigo C, Migliardi G, et al. Plasma risperidone concentrations during combined treatment with sertraline. *Ther Drug Monit* . Published online 2004. doi:10.1097/00007691-200408000-00008

23. D'Arrigo C, Migliardi G, Santoro V, et al. Effect of fluvoxamine on plasma risperidone concentrations in patients with schizophrenia.*Pharmacol Res* . Published online 2005. doi:10.1016/j.phrs.2005.09.005

24. Azuma J, Hasunuma T, Kubo M, et al. The relationship between clinical pharmacokinetics of aripiprazole and CYP2D6 genetic polymorphism: Effects of CYP enzyme inhibition by coadministration of paroxetine or fluvoxamine. *Eur J Clin Pharmacol* . Published online 2012. doi:10.1007/s00228-011-1094-4

25. Nemoto K, Mihara K, Nakamura A, et al. Effects of escitalopram on plasma concentrations of aripiprazole and its active metabolite, dehydroaripiprazole, in Japanese patients. *Pharmacopsychiatry* . Published online 2014. doi:10.1055/s-0034-1372644

26. Gossen D, de Suray JM, Vandenhende F, Onkelinx C, Gangji D. Influence of fluoxetine on olanzapine pharmacokinetics. *AAPS PharmSci* . Published online 2002. doi:10.1208/ps040209

Appendices

Table 1. Potential CYP-mediated DDIs in the SSRI prescriptions

Table 2. The frequencies and percentages of potentially CYP450-mediated DDIs for each SSRI

Table 3. The frequencies and percentages of potentially CYP450-mediated DDIs in category D&C

Table 4. The most five prescribed potentially interacted drug combinations and affected CYP450 isozymes for category D&C

Table 5. The frequencies and percentages of affected CYP450 isozymes in the prescriptions with pDDIs

Table 6. The frequencies and percentages of the most frequently potentially CYP450-interacted drugs with SSRIs and alternative SSRIs for remove CYP450-mediated DDIs

Figure 1. The most frequently potentially CYP450-mediated interacted drug groups with SSRIs

Supplemental dataset

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